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ARTICLE



Suspension of fertility treatment during the COVID-19 pandemic: views, emotional reactions and psychological distress among women undergoing fertility treatment



BIOGRAPHY

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KEY MESSAGE

Anxiety related to COVID-19 and disagreement with the suspension of fertility treatment during the initial phase of the COVID-19 pandemic were found to be significantly associated with psychological distress among women undergoing fertility treatment. The long-term psychological effects of the pandemic on the infertile population need further study.

ABSTRACT

Research question: What are the views and emotional reactions of patients towards the suspension of fertility treatment during the COVID-19 pandemic, and what are the factors affecting their psychological distress?

Design: A cross-sectional study conducted in an academic fertility centre. Online questionnaires were distributed between 18 April 2020 and 23 April 2020 to patients whose treatment cycle had been postponed or discontinued. The outcome measures included agreement with the reproductive society guidelines to postpone treatments; willingness to resume treatments, given the choice; patients' emotional reactions; and psychological distress level, measured by the Mental Health Inventory validated scale. A multivariate linear regression was conducted to identify factors associated with psychological distress.

Results: Because of the small number of male respondents, only women were included in the analysis ($n = 181$). Forty-three per cent expressed disagreement with the guidelines and 82% were willing to resume treatments, given the choice. Sadness and anxiety were the most common emotional reactions expressed towards the guidelines. In the multivariate analysis, COVID-19-related anxiety ($B = 0.145$, $P = 0.04$) and disagreement with treatment suspension ($B = -0.44$, $P = 0.001$) were found to be significantly associated with patients' psychological distress. Background characteristics of patients did not contribute significantly to their distress.

Conclusions: Suspension of fertility treatment during the initial phase of the COVID-19 pandemic was associated with patients' negative emotional reactions. Anxiety related to COVID-19 and disagreement with treatment suspension were found to be significantly associated with psychological distress among women undergoing fertility treatment, regardless of their background characteristics. Our findings suggest the need to monitor the mental health of patients and provide psychological support should a shutdown of fertility care re-occur.

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KEYWORDS

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INTRODUCTION

Since it was first recognized in Hubei Province, China, in December 2019, the novel Coronavirus Infectious Disease (COVID-19) has spread rapidly throughout the world, leading the World Health Organization, on March 2020, to declare a pandemic (WHO, 2020). Facing a rapidly evolving emergency, most countries implemented outbreak control measures, including travel restrictions and border closure, social distancing, closure of educational and employment facilities and wide-scale quarantines (Anderson et al., 2020). The outbreak affected all medical fields, resulting in the formulation of new clinical guidelines for each, based on public health directives. This included suspension of all non-urgent care, averting further strains on the medical system, while enabling reallocation of healthcare resources to COVID-19 care (CDC, 2020).

On the basis of the aforementioned public health considerations put forth by the World Health Organization, and the lack of data on the effect of maternal infection in the first and second trimesters on pregnancy and neonatal outcomes (Chen et al., 2020; Dong et al., 2020; Li et al., 2020; Yu et al., 2020), the reproductive medicine scientific societies opted for a cautionary approach towards medically assisted reproduction (MAR) treatments. On 17 March 2020, The American Society for Reproductive Medicine (ASRM), issued practice recommendations in line with the new public health strategies. They recommended that clinics suspend all new MAR treatment cycles, including initiation of ovulation induction with timed intercourse, intrauterine insemination, In Vitro Fertilization (IVF) and embryo transfer cycles. They excluded cycles of fertility preservation treatments for oncology patients about to undergo gonadotoxic therapies (ASRM, 2020). Similar recommendations were issued by the European Society of Human Reproduction and Embryology (ESHRE) and the Canadian Fertility and Andrology Society (CFAS), as well as most other fertility organizations in the world, during the month of March 2020 (CFAS, 2020; Cochrane, 2020; ESHRE, 2020).

It is well known that large-scale human disasters, such as global pandemic diseases, natural disasters, war conflicts

and social crises, can lead to massive stress-related disorders in the population affected (Lee et al., 2007; Ćosić et al., 2020). Similar effects on the mental health of the general population were demonstrated during the current outbreak. In a survey conducted in China during the early phase of the COVID-19 outbreak, more than one-half of the respondents rated the psychological effect on them as moderate-to-severe and about one-third reported moderate-to-severe anxiety (Wang et al., 2020). Studies evaluating the psychological effects of the COVID-19 pandemic on the infertile population, however, are scarce.

Infertility affects the psychological, relational and emotive aspects of the lives of most fertility patients, and is often described as their most stressful life event (Klonoff-Cohen et al., 2001; Slade et al., 2007). Fertility treatments place physical, economical and emotional burdens on couples, hence serving as a major stress factor (Cwikel et al., 2004; El Kissi et al., 2013). Several adaptive coping strategies, including problem-focused coping, emotional processing and expression and positive reappraisal (Stanton, 1991; Berghuis and Stanton, 2002; Lancaster et al. 2008; Musa et al., 2014; Ockhuijsen et al., 2014), as well as social support (Peterson et al., 2006; Martins et al., 2011), were found to help mitigate psychosocial distress and serve as potential protective mechanisms.

The outbreak, as well as the response, imposed unprecedented negative social and psychological effects on the general population, including fear of infection and its consequences, frustration, anger, anxiety and depression, social isolation due to large-scale quarantines and financial uncertainty (Brooks et al., 2020; Rodríguez-Rey et al., 2020). The unique circumstances of the COVID-19 pandemic, together with the unexpected suspension of fertility treatments, could aggravate the psychological and emotional distress of the fertility patients, hence it was important to assess the mental health of this susceptible population. Data on the effect of treatment suspension on the fertility population during the current pandemic are limited. A survey conducted in New York, USA, demonstrated that most of the respondents were very upset by the cancellation of fertility treatments (Turcoy et al. 2020). Another study from the UK

found that patients appraised fertility clinic closure as having potential for a more negative than positive effect on their lives and to be very uncontrollable and stressful (Boivin et al., 2020).

The aims of the present study based in Canada were to investigate the views and emotional reactions of patients towards the reproductive society (CFAS) guidelines; assess the variables associated with patients' views; and evaluate the factors contributing to psychological distress experienced by fertility patients in this challenging situation.

MATERIALS AND METHODS

Study design

This questionnaire-based, mixed-methods study was conducted at CReATe Fertility Centre, a large fertility centre in Toronto, Canada. A cross-sectional and descriptive design was chosen owing to the lack of empirical data on the experience of suspension of fertility treatment during previous outbreaks, and to assess the views, emotional reaction and psychological distress of patients at this limited period of time during the current pandemic. The study protocol was approved by the VERITAS Research Ethics Board on 16 April 2020 (IRB#16553) before data collection.

Participants

All patients, either female or male partner and single women, aged 18–54 years, with a valid email address, whose fertility treatment cycle had been postponed or discontinued after publication of the COVID-19 CFAS guidelines (CFAS, 2020), were included in the study. Gestational carriers as well as oocyte donors were excluded.

Data collection

The questionnaire, designed and distributed via the google-forms platform, was sent by email to the study population. Patients received an email message with a written explanation about the study and a request that the questionnaire should be completed by only one partner. Consent to participate was obtained before the survey was initiated. The survey was distributed to a total of 464 patients between 18 April and 23 April 2020. Data were collected anonymously until 7 May 2020, before the reopening of our clinic. A total of 187 surveys were collected and, of these, six were completed by patients who were in

a same-sex male relationship. Because of the small number of men who completed the survey, only women were included in the final analysis ($n = 181$).

Questionnaire

The questionnaire was constructed and reviewed by a team of reproductive physicians, psychologists and other health professionals based on clinical experience and a literature review. It included 65 self-administered questions and consisted of five parts. The four main outcome variables were agreement with the CFAS guidelines to postpone initiation of new fertility treatments (yes, no); willingness to resume treatments, if given the choice (yes, no); patients' emotional reactions to the guidelines; and psychological distress level as measured by the Mental Health Inventory (MHI-5) validated scale (description of the MHI-5 scale will follow below).

The first part consisted of questions addressing the demographics and infertility history of participants, and the second part included questions about occupational and lifestyle modifications resulting from the COVID-19 pandemic. Financial concerns caused by the current situation, as well as their potential effect on future resumption of treatment, were also addressed.

The third part consisted of five items evaluating COVID-19-related anxiety and COVID-19 social support, yielding two scores: (A) COVID-19-related anxiety score consisting of three items: being infected by the COVID-19; a family member being infected by COVID-19; and visiting a clinic or hospital for examination. Respondents' anxiety level was marked on a five-point Likert scale. The final score was calculated by averaging the patient responses to all three questions, with higher scores indicating greater anxiety (Cronbach's alpha was 0.78); and (B) COVID-19 social support score, consisting of two items evaluating perceived support from family and friends. Patients' responses to these questions were ranked on a five-point Likert scale. The score was formulated based on the average of patient responses to both items (Cronbach's alpha was 0.65).

The fourth part of the questionnaire assessed the views and emotional reactions of participants to the guidelines about suspending treatments. First,

patients were asked whether they believed the decision to suspend all fertility treatments was justified and, second, whether they would resume treatment, if given the choice. They were also asked to specify the main reason, in their opinion, for treatment suspension and, in case they did not wish to resume treatment, the main reason for this decision. Next, patients were asked to note their main feelings in response to the CFAS guidelines. The choices included anger, helplessness, anxiety, sadness, confusion and relief.

The last part included evaluation of wellbeing and distress using the MHI-5 (Stewart *et al.*, 1988), and comprised five items relating to the participant's wellbeing, e.g. 'I felt relaxed and stress-free', and distress, e.g. 'I felt sad and upset' during the past week. Responses were rated on a six-point scale, ranging from 1 ('never') to 6 ('all the time'). In this section, Cronbach's alpha was 0.78. The total score was calculated by averaging the responses to all five items, with a higher score reflecting greater psychological distress.

Data analysis

Qualitative analysis

Comments were imported into Excel spreadsheets for thematic analysis (Vaismoradi *et al.*, 2013; Chapman *et al.*, 2015). Investigator triangulation was achieved by organizing the data, identifying recurrent themes and labelling the contents using codes through an iterative process. The codes were then reviewed by LMH and AKS from the research team to inform the development of commonalities, emergent categories, underlying sub-themes and interrelated patterns using constant comparative methods (Strauss and Corbin, 1998). Differences were resolved through revision and discussion until consensus was reached. The data were then presented in a thematic map of a visual presentation of themes, sub-themes and categories to capture the main reasons for participants' views on the guidelines and resuming fertility treatment, given the choice.

Quantitative analysis

Statistical Package for Social Sciences version 26 was used for all analyses. Chi Squared or Fisher's exact, t-tests and analysis of variance with post-hoc tests were used, as appropriate, to

compare the differences between the study variables. Appropriate correlations were used to evaluate associations between the study independent variables. Point-biserial correlations were used to examine relationships between continuous variables and key bivariate variables.

Univariate analysis

As this is a new area of study, lacking previous empirical data, a univariate analysis between all the study variables and the dependent variable MHI-5 was conducted to look for variables that showed significant association with the outcome measure.

Multivariate analysis

Significant variables were then entered into a forward multivariate linear regression model predicting psychological distress. The aim was to preserve power while identifying the most parsimonious model and the variables associated with psychological distress. Finally, a forward entry linear regression was used for subgroup analysis according to the attitude to the guidelines (agreement versus disagreement). $P < 0.05$ was considered statistically significant.

RESULTS

One hundred and eighty-one women completed the survey for a response rate of 40%. Mean age of the participants was 37.7 years (SD = 4.6, range 29–54 years). The characteristics of the participants are presented in TABLE 1. Most participants (70%) had no children. Seventy-six per cent of respondents were planning to start an IVF or frozen embryo transfer cycle, whereas the remaining were planning to start intrauterine insemination or ovulation induction treatments. Ninety-three per cent of participants had a partner, about one-half had a postgraduate education and 61% reported an above average household income level ($\geq 110,000$ CAD). A large proportion of the study population (81%) was currently working, but about one-half foresaw an income loss in the upcoming period. Most (82%), however, reported that a foreseeable income loss would not affect their plan to resume treatments.

Participants' attitude towards the CFAS guidelines were as follows: 43% disagreed and the majority (82%) were willing to resume treatments, if they were given the

TABLE 1 CHARACTERISTICS OF WOMEN UNDERGOING FERTILITY TREATMENT AND COVID-19-RELATED VARIABLES ACCORDING TO AGREEMENT WITH THE CFAS GUIDELINES AND WILLINGNESS TO RESUME TREATMENTS

Socio-demographic and infertility characteristics	All	Agree with the CFAS guidelines		P-value	Willing to resume treatments		P-value
	(n = 181)	No (n = 78)	Yes (n = 103)		No (n = 33)	Yes (n = 148)	
Age, years ^a , n (%)				0.28			0.03
<35	40 (22)	14 (18)	26 (25)		10 (30)	30 (20)	
35–40	97 (54)	47 (60)	50 (49)		11(33)	86 (58)	
≥41	44 (24)	17 (22)	27 (26)		12 (36)	32 (22)	
Education ^a , n (%)				0.34			0.60
High School	4 (2)	3 (4)	1 (1)		1 (3)	3 (2)	
Community college	23 (13)	7 (9)	16 (16)		5 (15)	18 (12)	
Undergraduate	65 (36)	27 (35)	38 (37)		9 (27)	56 (38)	
Postgraduate	89 (49)	41 (53)	48 (47)		18 (55)	71 (48)	
Income, CAD ^a , n (%)				0.005			0.31
<109,999	51 (28)	14 (18)	37 (36)		14 (42)	37 (25)	
≥110,000	110 (61)	56 (72)	54 (52)		17 (52)	93 (63)	
Prefer not to say	20 (11)	8 (10)	12 (12)		2 (6)	18 (12)	
Relationship ^a , n (%)				0.40			0.99
Single	13 (7)	4 (5)	9 (9)		2 (6)	11 (7)	
Has a partner	168 (93)	74 (95)	94 (91)		31 (94)	137 (93)	
Number of children ^a , n (%)				0.33			0.68
0	127 (70)	58 (74)	69 (67)		22 (67)	105 (71)	
≥1	54 (30)	20 (26)	34 (33)		11 (33)	43 (29)	
Religious, status ^a , n (%)				0.1			0.93
Religious	78 (43)	39 (50)	39 (38)		14 (42)	64 (43)	
No religion	103 (57)	39 (50)	64 (62)		19 (58)	84 (57)	
Occupation ^a , n (%)				0.78			0.54
Health-related	46 (25)	19 (24)	27 (26)		7 (21)	39 (26)	
Other	135 (75)	59 (76)	76 (74)		26 (79)	109 (74)	
Ethnicity ^a , n (%)				0.43			0.11
White	115 (64)	47 (60)	68 (66)		17 (52)	98 (66)	
Non-white	66 (36)	31 (40)	35 (34)		16 (48)	50 (34)	
Infertility diagnosis ^a , n (%)				0.04			0.42
Female factor	66 (36)	35 (45)	31 (30)		10 (30)	56 (38)	
Other	115 (64)	43 (55)	72 (70)		23 (70)	92 (62)	
Fertility treatment ^a , n (%)				0.16			0.39
IUI or ovulation induction	43 (24)	15 (19)	28 (27)		6 (18)	37 (25)	
IVF	74 (41)	38 (49)	36 (35)		12 (36)	62 (42)	
FET	64 (35)	25 (32)	39 (38)		15 (45)	49 (33)	
Treatment length, years ^a				0.28			0.70
Up to 1	102 (56)	39 (50)	63 (61)		18 (55)	84 (57)	
1–2	40 (22)	21 (27)	19 (18)		9 (27)	31 (21)	
>2	39 (22)	18 (23)	21 (20)		6 (18)	33 (22)	
IVF cycles, n ^a				0.17			0.09
0	32 (26)	17 (29)	15 (24)		4 (17)	28 (28)	
1–2	60 (49)	24 (41)	36 (57)		16 (70)	44 (44)	
≥3	30 (25)	18 (31)	12 (19)		3 (13)	27 (27)	

(continued on next page)

TABLE 1 (continued)

Socio-demographic and infertility characteristics	All	Agree with the CFAS guidelines		P-value	Willing to resume treatments		P-value
	(n = 181)	No (n = 78)	Yes (n = 103)		No (n = 33)	Yes (n = 148)	
Total	122 (100)						
COVID-19-related variables							
Currently working ^a				0.10			0.09
Yes	146 (81)	63 (81)	83 (81)		23 (70)	123 (83)	
No, laid off	16 (9)	7 (9.0)	9 (9)		3 (9)	13 (9)	
No, not working before	19 (10)	8 (10)	11 (11)		7 (21)	12 (8)	
Any anticipated income loss ^a				0.69			0.99
Yes	99 (55)	44 (56)	55 (53)		18 (55)	81 (55)	
No	82 (45)	34 (44)	48 (47)		15 (45)	67 (45)	
COVID-19 anxiety scale, mean (SD) ^b	2.74 (0.90)	2.45(0.84)	2.95 (0.88)	<0.001	3.30 (0.79)	2.61 (0.87)	<0.001
COVID-19 social support scale, mean (SD) ^b	3.38 (0.81)	3.21 (0.83)	3.52 (0.77)	0.009	3.65 (0.70)	3.32 (0.82)	0.03

Percentages have been rounded and may not total to 100%.

^a Chi-squared test.

^b t-test. CAD, Canadian dollar; CFAS, Canadian Fertility and Andrology Society; FET, frozen embryo transfer; IUI, intrauterine insemination.

choice. Participants' characteristics and COVID-19-related variables according to their agreement or disagreement with the CFAS guidelines and willingness or unwillingness to resume treatments are also presented in TABLE 1. Income and infertility diagnosis differed significantly according to agreement with the guidelines: a significantly higher proportion of women in the higher income group disagreed with the guidelines compared with the lower income group (56/110 [51%] versus 14/51 [27%], chi-squared = 7.8, $P = 0.005$); women with female factor infertility compared with other infertility diagnosis (35/66 [53%] versus 43/115 [37%], chi-squared = 4.2, $P = 0.04$). In addition, a significantly greater proportion of women aged 35–40 years were willing to resume treatments compared with women in the other age groups (chi-squared = 6.7, $P = 0.03$).

Most participants expressed feelings of sadness (66%), followed by anxiety (60%) and helplessness (60%) in response to the CFAS guidelines. Nevertheless, only one in 10 participants expressed confusion about the guidelines. As shown in TABLE 1, participants who agreed with the guidelines had a higher COVID-19 anxiety score (2.95 versus 2.45, $t = -3.91$, $P < 0.001$) as well as those who were unwilling to resume treatments (3.30 versus 2.61, $t = 4.12$, $P < 0.001$). In addition, a higher level of COVID-19 social support was found in women who agreed with the guidelines (3.52 versus

3.21, $t = -2.63$, $P = 0.009$), and in those who did not wish to resume treatments (3.65 versus 3.32, $t = 2.12$, $P = 0.03$).

The key themes extracted from the free-text comments of respondents in favour of and against treatment postponement and willingness to resume treatments, despite foreseeable income loss, are presented in TABLE 2. Reasons given in favour of postponement included prevention of infection; saving healthcare resources for COVID-19 treatment; and possible risks of maternal infection on the pregnancy. Conversely, reasons given against postponement included future strain on the resources of fertility clinics, such as increasing wait time for treatments; time sensitivity of fertility treatments; IVF is an essential medical service; and finding a way to keep performing fertility treatments safely. Reasons to resume treatment included prioritizing IVF; financial planning for IVF; and financial support from the family. Reasons not to resume treatment included inability to afford the treatments and financial uncertainty.

Before conducting a regression model, a univariable analysis was carried out that showed that disagreement with the guidelines ($t = 2.99$, $P = 0.003$) and lower COVID-19 social support ($r = 0.16$, $P = 0.03$) were significantly associated with higher psychological distress.

Forward regression model was then applied in two steps (TABLE 3). Step 1 was

insignificant, with none of the background variables contributing significantly to the psychological distress. Step 2 showed significant associations between the main variables: disagreement with the guidelines ($B = -0.44$, $P = 0.001$), greater COVID-19 anxiety ($B = 0.145$, $P = 0.041$) and distress.

As a result of the significant differences in the COVID-19 anxiety score, in agreement with the guidelines shown previously, a point-biserial correlation analysis was conducted, which showed a significant correlation between disagreement with the guidelines and COVID-19 anxiety ($r = 0.28$, $P < 0.001$). Next, a split regression analysis of COVID-19 anxiety by agreement with the guidelines was conducted, which showed a significant association between COVID-19 anxiety and distress only in the agreement group ($B = 0.9$, $P = 0.005$) and not the disagreement group ($P = 0.73$).

DISCUSSION

More than 6 months since its onset, the COVID-19 pandemic continues to affect the world with an increasing number of cases and over 2,000,000 deaths worldwide (*WHO Coronavirus Disease [COVID-19] Dashboard*, 22.01.21). Resurgence of cases in those countries that loosened their restrictions early, i.e. reopening businesses and workplaces, has even created the need to re-impose mitigation measures.

TABLE 2 FREE-TEXT COMMENTS OF RESPONDENTS ON THEIR ATTITUDES TO THE CFAS GUIDELINES AND WILLINGNESS TO RESUME TREATMENTS

Topic	Key themes	Categories	Illustrative quotes
Agreement with the CFAS guidelines	Reasons in favour of postponing the treatments	Prevent infection	'Between having a baby and saving lives by stopping the spread, saving lives comes first, hands down.'
		Save the healthcare resources for COVID-19 care	'I would move forward if it were an option, but would feel guilty if personal protective equipment (PPE) were used for my transfer that was needed elsewhere.'
		Possible risks of coronavirus infection on embryo development and the pregnancy	'I'm scared of getting COVID-19 while being pregnant.'
Disagreement with the CFAS guidelines	Reasons against postponing the treatments	Future strain on the fertility clinics	'No reason to postpone. There has to be a way to solve this. This will create further strain on the system and only add to the wait times.'
		Time sensitivity of fertility treatments	'These are TIME SENSITIVE treatments! If my IVF treatments do not end up being successful, I will ALWAYS wonder what role having IVF treatments postponed during the COVID-19 pandemic played.'
		IVF is an essential medical service	'There are many facing time constraints, fertility treatment is not elective.'
		Find a way to keep performing fertility treatment safely	'Fertility clinics should be able to continue to conduct fertility treatments that are safe for both patients and medical professionals. Delayed treatment is only adding to an already difficult situation. Please don't compromise the future of parents and families.'
Willingness to resume treatments	Finance for fertility treatments - in case of foreseeable income loss	Fertility is prioritized	'Becoming pregnant is a priority we cannot postpone.'
		Financial planning for IVF	'We planned this before COVID, so we have money saved aside for the treatment.'
		Financial support from the family	'We are fortunate enough to have family who can help if we cannot afford it ourselves.'
Unwillingness to resume treatments		Inability to afford treatments	'Won't be able to afford fertility treatments.'
		Economic uncertainty	'I will try my best to provide monetarily, but the future is unknown.'

CFAS, Canadian Fertility and Andrology Society.

At the beginning of the pandemic, many fertility scientific societies worldwide recommended suspension of all non-urgent fertility treatments for an indefinite period of time (ASRM, 2020; CFAS, 2020; ESHRE, 2020), leaving the infertility population with great

uncertainty. The objective of the preset study was to capture the attitudes and emotional reactions of patients to this shut down, as well as to evaluate variables contributing to their psychological distress during this unprecedented situation.

Our findings suggest that almost one-half (43%) of participants disagreed with the guidelines and most would have liked to resume treatment, despite the increasing rates of infection and limited data on the effects of COVID-19 infection during pregnancy.

TABLE 3 FORWARD LINEAR REGRESSION MODEL FOR PSYCHOLOGICAL DISTRESS

	Beta (95% CI)	P-value	Adjusted R ²	F	Effect size (f ²)
Step 1: demographic variables not entered into model					
Overall	–				
Age	–	NA			
Previous IVF (yes, no)	–				
Treatment length (≤1year, 1–2 years, >2 years)	–				
Infertility diagnosis (female factor, other)	–				
Step 2:					
Overall		0.002	0.06	6.7	0.075
Agreement with the guidelines	–0.443 (–0.693 to –0.192)	0.001	0.06	6.7	0.08
COVID-19 anxiety	0.145 (0.006 to 0.284)	0.041			
Variables not entered into model					
Willingness to resume treatments	–				
COVID-19 social support	–				

NA, not applicable.

Previous recent studies demonstrated similar results on patients' views towards treatment suspension. A survey conducted in New York, USA, at the beginning of the pandemic found that 86% of patients preferred to have the option to start treatments in consultation with their physician, and 58% chose to resume, given the option (Turcoy *et al.*, 2020). In another study, evaluating the effect of the COVID-19 pandemic on fertility patients, only 6% of the participants declared that fertility treatments, including IVF, should be postponed (Vaughan *et al.*, 2020). Interestingly, in our study, participants' statements in favour of treatment postponement were similar to the reasons stated in the guidelines, including prevention of infection, saving healthcare resources for COVID-19 care and possible risks of infection during pregnancy. The statements of participants against postponement and in favour of resuming treatments demonstrated concern about the future strain on fertility clinics, age-related time sensitivity of treatments, in addition to asserting that IVF is an essential medical service and, therefore, a safe way to continue fertility treatments needs to be found.

Higher household income, as well as female factor infertility, were found to be significantly associated with disagreement with the guidelines. Previous studies, in non-pandemic times, have shown disparities in the access and use of fertility care according to socioeconomic status in the USA, in which, as in Canada, fertility services and MAR treatments are characterized by high underinsurance rates and high out of pocket expenditure (Adashi and Dean, 2016; Kelley *et al.*, 2019). Moreover, financial concerns are important factors affecting the decision not to pursue treatment after the initial diagnosis (Eisenberg *et al.*, 2010). The pandemic contributed to financial instability owing to increased rates of unemployment (International Labor Organization, 2020). Hence, patients with lower income tended to agree with the guidelines compared with patients with higher income, possibly owing to concerns about the ability to pay for the treatments as well as their future financial security.

Age was the only background characteristic associated with the desire to resume treatments, with

higher rate of women at the age of 35–40 years willing to resume. Data on the variables associated with the will to resume treatment during the COVID-19 pandemic are limited. A recent study, conducted in Israel, demonstrated that shorter duration of treatment was the only variable found to be significantly associated with the wish to resume treatments during the current pandemic (Ben-Kimhy *et al.*, 2020). The sociocultural difference between the Israeli and the present study population, however, might limit the generalizability of the results. Increased women's age and perceived poor prognosis were previously shown to be associated with unwillingness to pursue fertility treatment (Malcolm and Cumming, 2004; Eisenberg *et al.*, 2010). Moreover, both the marked decline in fecundability demonstrated in women aged 35–40 years (Rothman *et al.*, 2013), and the reduced success rates of MAR treatments after the age of 35 years (Committee opinion of American Society for Reproductive Medicine, 2014), might explain our observation that women aged 35–40 years feel more pressure to resume treatment owing to time sensitivity, whereas older women are less keen to resume treatment owing to poor prognosis. Because of the lack of previous experience of treatment suspension during outbreaks, further studies are needed to establish this observation.

Higher COVID-19-related anxiety was associated with unwillingness to resume treatments. Previous studies demonstrated a range of psychological effects and emotional reactions of people during outbreaks, such as fear of infection, falling sick or dying (Hall *et al.*, 2008; Rubin *et al.*, 2010). A large recent study, from the early phase of the COVID-19 pandemic, showed that most respondents were concerned about family members contracting COVID-19, with higher concern associated with higher anxiety and stress scores (Wang *et al.*, 2020). According to the present study, although fertility patients made the decision, before the pandemic, to undergo fertility treatments, anxiety related to the pandemic had a negative effect on their decision to continue pursuing parenthood.

Assessment of the parameters that contributed to participants' distress in our study showed that none of their

background characteristics contributed significantly to their psychological distress. Infertility diagnosis and fertility treatments themselves are associated with increased psychological stress, anxiety and depression (Matsubayashi *et al.*, 2001; Sbaragli *et al.*, 2008). Moreover, stress levels have been shown to be similar to those of patients with life-threatening medical illnesses, such as cancer and heart disease (Domar *et al.*, 1993). Increased age, longer duration of infertility, previous fertility treatments and female factor infertility have been shown to be associated with higher stress levels in infertile women in previous studies (Domar *et al.*, 1992; Ogawa *et al.*, 2011; Patel *et al.*, 2016; Zaidouni *et al.*, 2018). Interestingly, our findings reflected those of Ben Kimhy *et al.* (2020), which demonstrated that women's background characteristics were not as prominent predictors for distress, as the pandemic itself, together with the abrupt suspension of treatments.

Furthermore, most participants expressed negative feelings in response to the CFAS guidelines. Of note, only one in 10 of the respondents felt confused, suggesting that most of the respondents understood the guidelines and confusion did not play a major part in their emotional reaction. A previous study by Boivin *et al.* (2020) showed similar emotional reaction to clinic closure with more negative than positive emotions reported by the survey participants (Boivin *et al.*, 2020). Disagreement with the guidelines and higher COVID-19-related anxiety were significantly associated with higher distress. Further regression analysis, split by agreement with the guidelines, showed that anxiety related to COVID-19 was associated with increased psychological distress, but only among women who agreed with the guidelines. Therefore, negative attitudes toward the guidelines, independent of the anxiety caused by the pandemic, were associated with higher distress.

Social support has a significant effect on the health and social functioning of each individual (Landman-Peeters *et al.*, 2005; Verhaak *et al.*, 2005). It serves as a protective factor against stress, reducing anxiety and depression levels, in both the infertile and fertile population (Landman-Peeters *et al.*, 2005; Erdem *et al.*, 2014). In our study, women's perceived social support affected their views towards

the guidelines. A higher COVID-19 social support score was associated with greater acceptance of the guidelines and unwillingness to resume treatment. Despite this, COVID-19 social support was not significantly associated with distress in the multivariate analysis.

A strength of the present study is that all participants were affected by treatment suspension as a result of the guidelines, which contributes to the reliability of our results. In addition, the use of a validated scale to assess the patients' psychological distress increases the confidence in our findings and the external validity of our results. Several limitations, however, also need to be considered. First, our study includes patients from a single large fertility centre located in a large urban area, in one country, which might limit the generalizability of our results. Second, because of clinic closure and avoidance of non-urgent visits, the questionnaires were distributed only via an online platform, which might have dissuaded those with limited computer skills from participating. Third, the questions were written in English, hence only applying to English speakers, which may not reflect the actual demographics of our population. Moreover, about one-quarter of the study population engaged in a health-related occupation. This population might be keener to participate, contributing to the limitation of the generalizability of our findings. Fourth, male population, either same-sex couples or heterosexual partners, was not represented in this study, owing to the small number of male participants. Previous studies showed different emotional reactions and stress between men and women (*Slade et al., 2007; El Kissi et al., 2013*), hence it is important in future research to evaluate the effects on a predominantly male population. Finally, we do not have information on the characteristics of the non-responders because of the anonymity of response, which might contribute to a selection bias. However, the mean age of respondents did not differ significantly from that of the overall study population, and the anonymity of response is a strength as it could reduce some types of response bias, e.g. social desirability and fear of response.

Notwithstanding the above limitations, our study provides invaluable information about the female fertility population facing an unprecedented event of fertility

clinic closures during the COVID-19 outbreak. The abrupt cessation of fertility treatments for an indefinite period increased the emotional burden and affected the psychological distress of this vulnerable population, independent of the anxiety related to the pandemic itself. Moreover, postponement of treatment is one of the most frequently selected reasons for discontinuing treatment among patients (*Gameiro et al., 2012*), thus increasing the risk for abandoning the dream of parenthood.

These observations emphasize the importance of reaching out to the infertile population, offering psychological support, such as professional online counselling and support groups. Use of extensive communication strategies, such as delivering updates via phone, email or social media about preparations for clinic reopening and personal discussions of treatment plans to be initiated at clinic reopening, can help reduce patients' sense of uncertainty (*Boivin et al., 2020*). Making inquiries about one's coping resources, e.g. keeping busy, engaging in physical activity, social support and encouraging the use of coping strategies, such as distraction and positive reappraisal, have previously been shown to be useful in managing uncontrollable stressful experiences. These could promote better tolerance of the unpredictable situation as well as improve the patients' wellbeing (*Ockhuijsen et al., 2014; Boivin et al., 2020*). Early interventions, as described above, might help mitigate foreseeable negative effects on patients' mental health in future outbreaks of COVID-19 or other calamities. Future longitudinal studies evaluating the wellbeing of fertility patients, both men and women, over time, conducted during routine and complex times, will enable further understanding of patients' experiences, evaluation of the variables affecting their mental health and assessment of causal relationships, all of which will help us provide tailored care for our patients.

In conclusion, the suspension of fertility treatment during the initial phase of the COVID-19 pandemic was associated with female patients' negative emotional reactions. COVID-19-related anxiety and negative attitudes towards treatment suspension were found to be significantly associated with psychological distress among women undergoing infertility treatment regardless of their background

characteristics. Recent experience of significant flares in the incidence of COVID-19 infection raises the concern that restrictive recommendations may need to be re-enacted in specific regions. Our findings suggest the need to closely monitor patients' mental health and provide psychological support should a shutdown of fertility care re-occur in the future.

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